

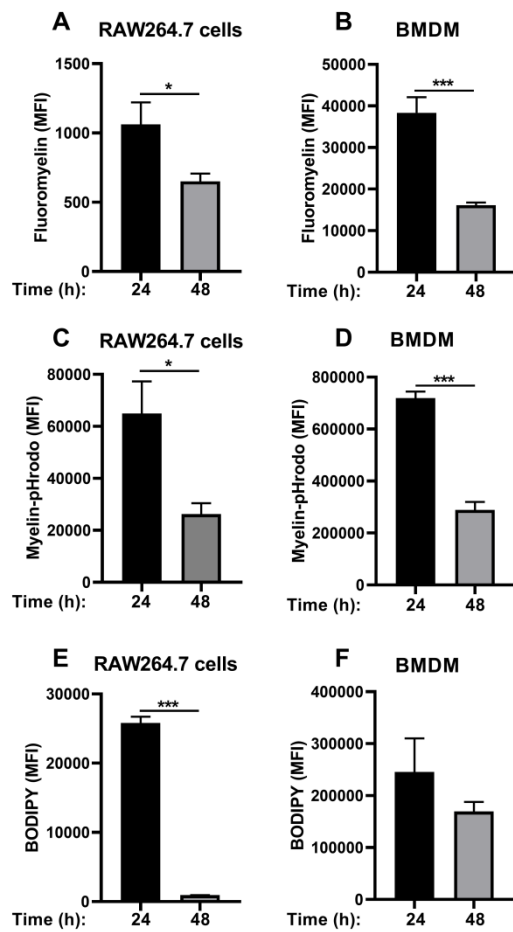


Fig. S1. Changes of intracellular myelin processing with time (MFI). RAW264.7 cells (A,C,E) or BMDM (B,D,F) were incubated with 50 $\mu\text{g/mL}$ myelin, followed by medium change and additional incubation of 24h or 48h. Median fluorescence intensity (MFI) was detected by flow cytometry. (A,B) Myelin labeled with FlouroMyelin was used to detect myelin accumulation inside the cells. (C,D) Myelin in acidic compartments (e.g. lysosomes) was detected by myelin labeled with pHrodo. (E,F) After the incubations, cells were stained with BODIPY 493/503 to detect neutral lipids. Results represent MFI means $\pm$ SEM of $n \geq 3$ independent experiments. Differences between the measurements at 24h and 48h after myelin withdrawal were highly significant in some cases (Student's t-test * $p < 0.05$, *** $p < 0.001$).

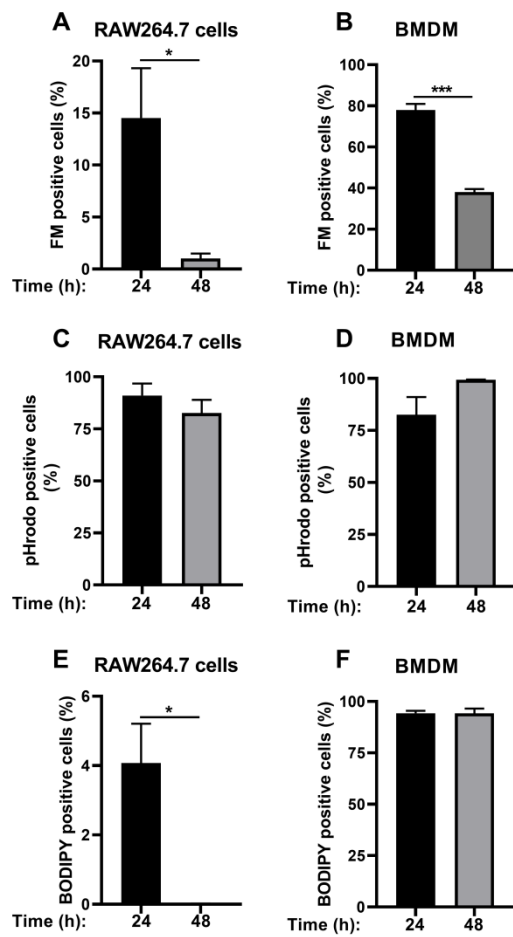


Fig. S2. Changes of intracellular myelin processing with time (percentage positive cells). RAW264.7 cells (A,C,E) or BMDM (B,D,F) were incubated with 50 $\mu\text{g}/\text{mL}$ myelin, followed by medium change and additional incubation of 24h or 48h. Percentage of fluorescence positive cells was detected by flow cytometry. (A,B) Myelin labeled with FlouroMyelin was used to detect myelin accumulation inside the cells. (C,D) Myelin in acidic compartments (e.g. lysosomes) was detected by myelin labeled with pHrodo. (E,F) After the incubations, cells were stained with BODIPY 493/503 to detect neutral lipids. Results represent cell percentage means $\pm$ SEM of $n \geq 3$ independent experiments. Differences between the measurements at 24h and 48h after myelin withdrawal were highly significant in some cases (Student's t-test * $p < 0.05$, *** $p < 0.001$).

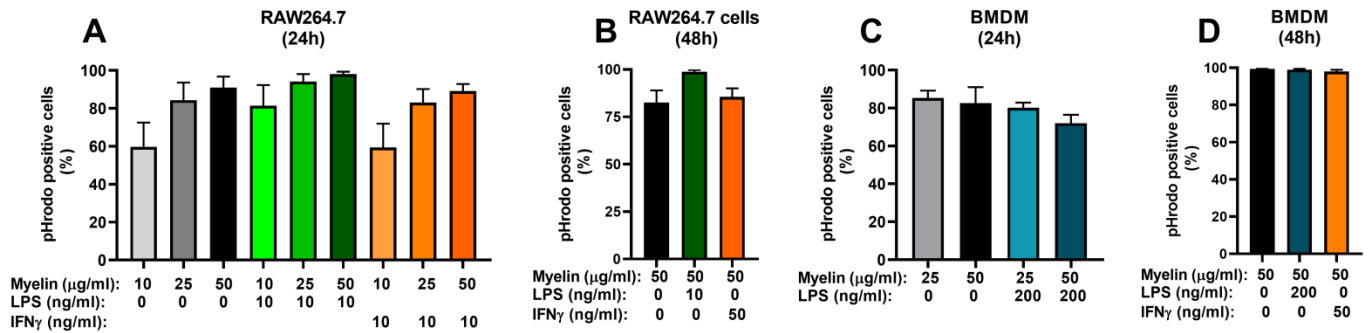


Fig. S3. Proportion of cells with lysosomal myelin fluorescence. RAW264.7 (A,B) or BMDM (C,D) were incubated with pHrodo-myelin at different concentrations (10, 25 or 50 μg/mL) for 24h. After washing non-phagocytosed myelin, cells were treated with LPS (10 or 200 ng/mL) or IFN γ (10 or 50 ng/mL) for additional 24h (A,C) or 48h (B,D). After this time, the percentage of pHrodo positive cells was determined by flow cytometry. Results represent means $\pm$ SEM of $n \geq 3$ independent experiments. Two-way ANOVA revealed significant effect in (A) $F(2,24)=8.46$, $p < 0.01$ in myelin concentrations, but Tukey's post-hoc test was not significant.

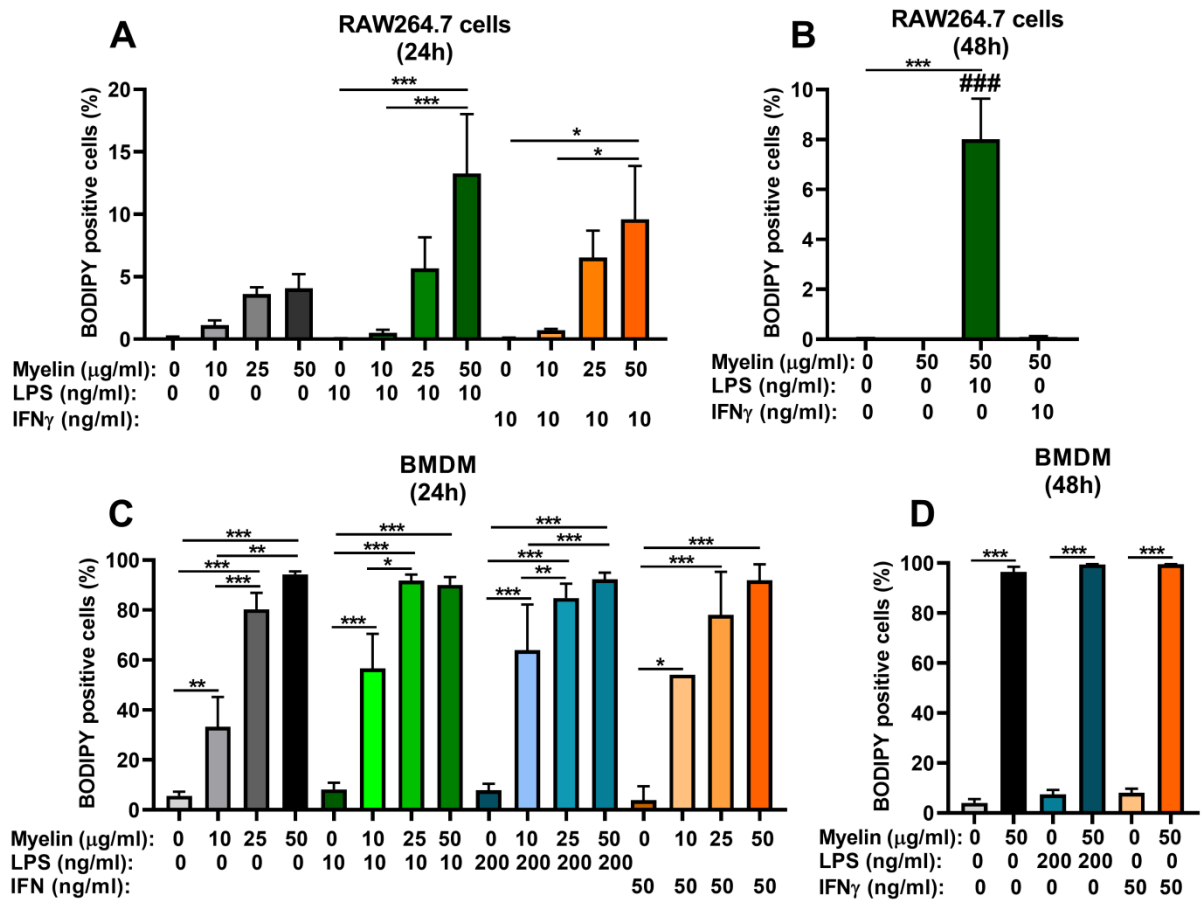


Fig. S4. Proportion of cells with BODIPY fluorescence. RAW264.7 (A,B) or BMDM (C,D) were incubated with myelin at different concentrations (10, 25 or 50 μg/mL for 24h. After washing non-phagocytosed myelin, cells were treated with LPS (10 or 200 ng/mL) or IFN γ (10 or 50 ng/mL) for additional 24h (A,C) or 48h (B,D) . After this time, cells were incubated with BODIPY 493/503 dye. The percentage of BODIPY positive cells was determined by flow cytometry. Results represent means $\pm$ SEM of $n \geq 3$ independent experiments. Two-way ANOVA revealed significant effect in (A) $F(3,36)=11.7$, $p < 0.001$, for myelin concentrations; (C) $F(3,83)=184.1$, $p < 0.001$ for myelin concentrations; and (D) $F(1,34)=5931$, $p < 0.001$ for myelin concentration; and $F(2,34)=3.79$, $p < 0.05$ for pro-inflammatory treatments. One-way ANOVA revealed significant effect in (B) $F(3,8)=23.80$, $p < 0.001$. Tukey's (A,C) or Sidak's (B,D) post-hoc test indicated statistical significance between treatments * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ and between 50 μg/mL of myelin and treatments (#).

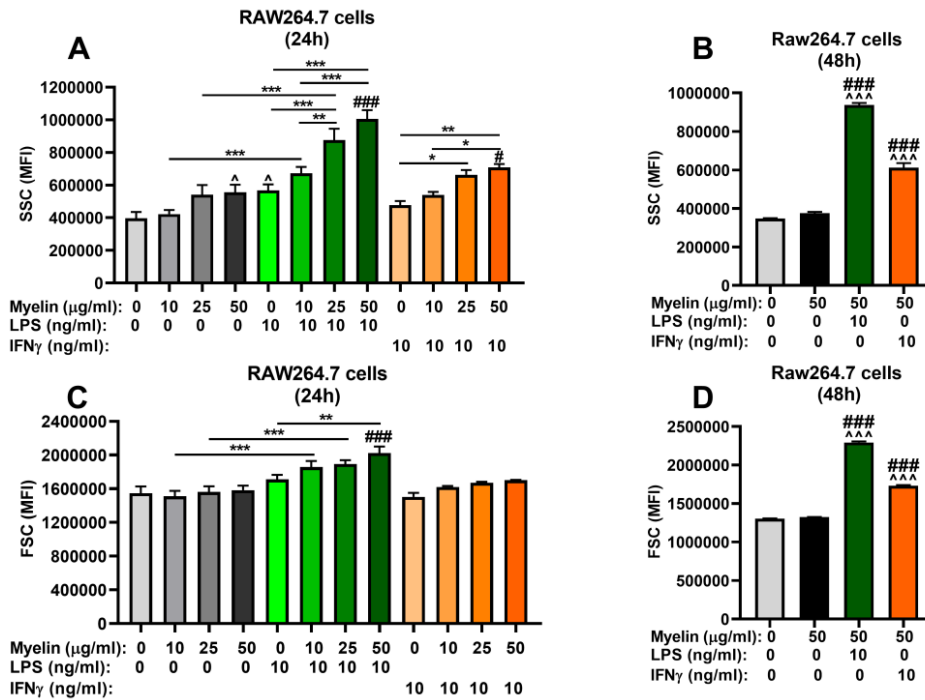


Fig. S5. Effect of myelin and pro-inflammatory stimuli on side-scatter (SSC) and forward scatter (FSC) in RAW264.7 cells. Cells were incubated with myelin at different concentrations (10, 25 or 50 μg/mL) for 24h. After washing non-phagocytosed myelin, cells were treated with 10 ng/mL of LPS or IFNγ for additional 24h (A,C) or 48h (B,D) . After this time, SSC (A,B) and FSC (C,D) was determined by flow cytometry. Results represent means ± SEM of n≥3 independent experiments. Two-way ANOVA revealed significant effect in (A) $F(3,36)=28.73$, $p<0.001$, for myelin concentrations and $F(2,36)=53.74$, $p<0.001$ for pro-inflammatory treatments and (C) $F(3,36)=5.609$ $p<0.01$ for myelin concentrations and $F(2,36)=36.06$ $p<0.001$ for pro-inflammatory treatments; One-way ANOVA revealed significant effect in (B) $F(3,8)=426.1$ $p<0.001$ and (D) $F(3,8)=3106$ $p<0.001$. Tukey's (A,C) or Sidak's (B,D) post-hoc test indicated statistical significance between treatments * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, between control and treatments (^) and between 50 μg/mL of myelin and treatments (#).

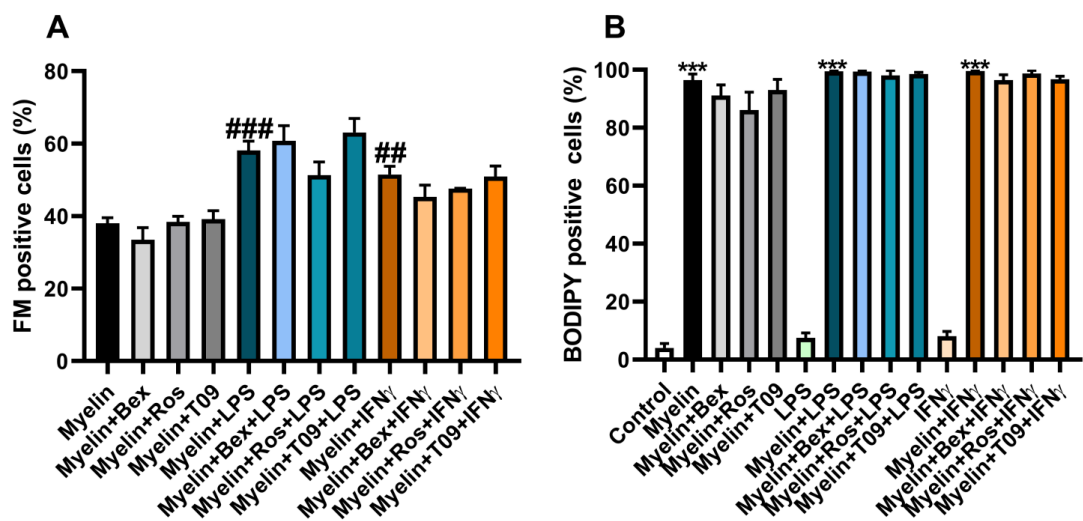


Fig. S6. Agonists of nuclear receptors reduced lipid accumulation in BMDM under pro-inflammatory condition. BMDM were incubated with myelin (50 $\mu\text{g}/\text{mL}$) for 24h. After washing non-phagocytosed myelin, cells were treated with LPS (200 ng/ml) or IFN γ (50 ng/ml) for additional 48h. After this time, cells were incubated with BODIPY 493/503 dye. The percentage of FM (A) or BODIPY (B) positive cells was determined by flow cytometry. Results represent means $\pm$ SEM of $n \geq 3$ independent experiments. One-way ANOVA revealed significant effect in (A) $F(11,55)=10.53$ $p < 0.001$ and (B) $F(14,39)=342.1$ $p > 0.001$. Sidak's post-hoc test indicated statistical significance between control and treatments *** $p < 0.001$ and between 50 $\mu\text{g}/\text{mL}$ of myelin and treatments ## $p < 0.01$ and ### $p < 0.001$.